



2019 ANNUAL REPORT



National Emerging
Infectious Diseases
Laboratories

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September 1, 2019

Letter from the Director

Last year, I started this letter by commenting that “Emerging Infectious Diseases, and the pathogens that cause them, continue to be in the headlines, almost on a daily basis”. This same statement rings true today, and these diseases will continue to be part of our daily news feed, if not our daily lives, for the foreseeable future. Just in this past year, we have seen the largest number of measles cases in the US in 25 years. Almost 1000 US residents contracted the disease, a sad fact given that measles can be (and had been as recently as the year 2000) eliminated due to the existence of an incredibly safe and effective vaccine. These facts alone underscore the importance of maintaining vaccine sufficiency in the population. Maintaining vaccinations are in many respects a social contract, protecting those who for health reasons cannot be safely vaccinated.

This year also saw outbreaks of a number of other emerging infectious diseases. One of these is “acute flaccid myelitis”, a polio like disease that primarily afflicts young children. Over 3 times more cases were diagnosed in 2018 (235) than in 2017, and the case counts continued to build in 2019. Cases have been identified in virtually every state. This illness is thought to be caused by one or more enterovirus, members of the picornavirus family (like the polio virus) that usually cause mild disease symptoms. How the viruses afflict the nervous system in a subset of patients is unclear, and understanding this obviously requires more work. As I write this letter, an outbreak of EEE virus (Eastern Equine Encephalitis virus) is occurring in Massachusetts and surrounding areas, as well as other parts of the US. This rare mosquito transmitted virus (an alphavirus) has no known effective therapy or vaccine, and is often not diagnosed until after the rapid onset of encephalitis. Finally, the second largest Ebola outbreak ever reported has been going on for over a year in the DRC, despite the fact there is now an apparently effective experimental vaccine that has been deployed to the region. To date, more than 200,000 persons have been inoculated, and yet the outbreak continues. Local events have significant impact on outbreak responses, which have substantial public health implications.

These and other regional outbreaks emphasize the importance of the work that is going on in the NEIDL. As we are still in the building phase, our focus has been on increasing the diversity of expertise in the NEIDL faculty and staff so that we can respond to the scientific and public health challenges that confront us. This past year has been devoted to building capacity, and expanding the expertise not only in the scientific arena, but also in our safety and facilities staffing. These professionals are who help make it possible for the scientific staff to do the work that is required of the scientific staff in a safe and secure manner.

Here are a few milestones from this past year.

We safely received two shipments of BSL-4 pathogens, following the transportation plans that were agreed upon with the City of Boston. Our environmental health and safety staff, as well as our security team, were instrumental in making this happen.

We recruited 2 new experienced BSL-4 investigators, Drs. Anthony Griffiths and Robert Davey. Both bring years of experience in studying pathogens such as Ebola virus, Marburg virus, and Lassa virus with them. They have both built impressive scientific teams to carry out their studies.

We also recruited 2 new investigators who work on “+ sense RNA viruses”, including important viruses such as flaviviruses and enteroviruses. The flaviviruses include pathogens that cause yellow fever, West Nile, Zika

and Dengue, to name a few. The enteroviruses I alluded to earlier. One virus that has been associated with acute flaccid myelitis is the enterovirus D68, and it can now be studied in the NEIDL. These two virologists will also work with Tonya Colpitts, whose insectary (for studying mosquito transmitted diseases) will be important for studying the natural mode of virus transmission. Mohsan Saeed joined us in March of 2019, and Florian Douam joined July 1.

We also had to say goodbye to an accomplished investigator, Paul Duprex, who was recruited as the Jonas Salk Chair for Vaccine Research at the University of Pittsburgh. This is a well-deserved accomplishment after an outstanding career with us at Boston University. We are proud of him and wish him the best.

The study of emerging infectious diseases often requires uniquely designed containment laboratories, facilities that are designed to keep laboratory workers safe while working with these pathogens. We have been permitted by both the Centers for Disease Control, and the Boston Public Health Commission, our main external regulators, to study pathogens that require biosafety level 3 (BSL-3) and BSL-4 containment, and as we add faculty it was imperative that we bring additional space on line for these studies. During this past year, in an effort led by our safety and facilities staff, we are now equipping additional suites of spaces that we had not yet occupied for these studies. These laboratories, along with the extensive BSL-2 spaces in the NEIDL, are devoted to understanding the emerging pathogens, the diseases they cause, and developing and testing improved diagnostics, therapeutics and vaccines for the public's health.

We also remain committed to being completely transparent about our work with the public. We do so in partnership with our Community Relations staff, who communicate with various community groups, help organize tours of the facility, keep our website current, and engage our Community Liaison Committee (CLC). CLC members advise us on strategies for communicating what we do, as well as helping us be innovative in how we can approach educational opportunities, including science, technology, engineering and math (STEM) education, in our neighborhoods. Some of these are highlighted in this annual report.



Ronald B. Corley, Ph.D.

Professor of Microbiology
Director, National Emerging Infectious Diseases Laboratories

Mission Statement and Strategic Plan

The Boston University National Emerging Infectious Diseases Laboratories (NEIDL) mission is to generate and translate fundamental knowledge on high priority emerging infectious diseases for the benefit of the public health, locally, nationally and globally.

Emerging infectious diseases are defined as those that have newly appeared and been recognized in the population, or have existed but are rapidly increasing in incidence or in geographic range. To meet our missions the NEIDL will:

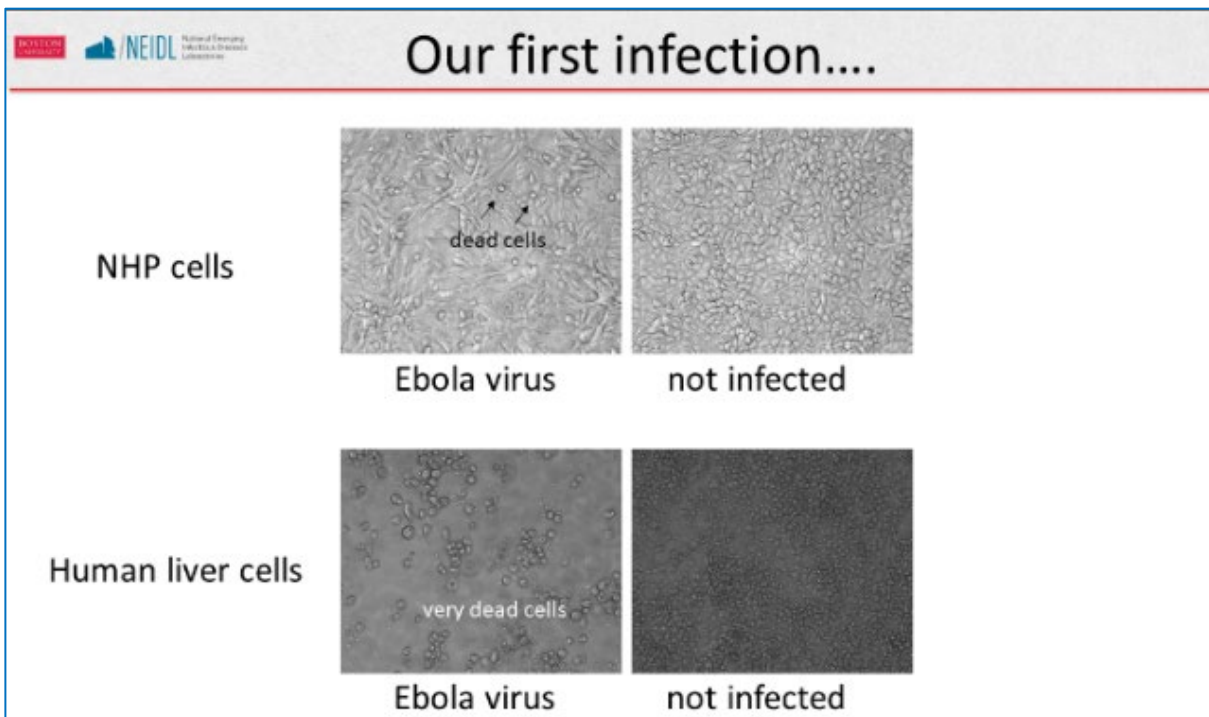
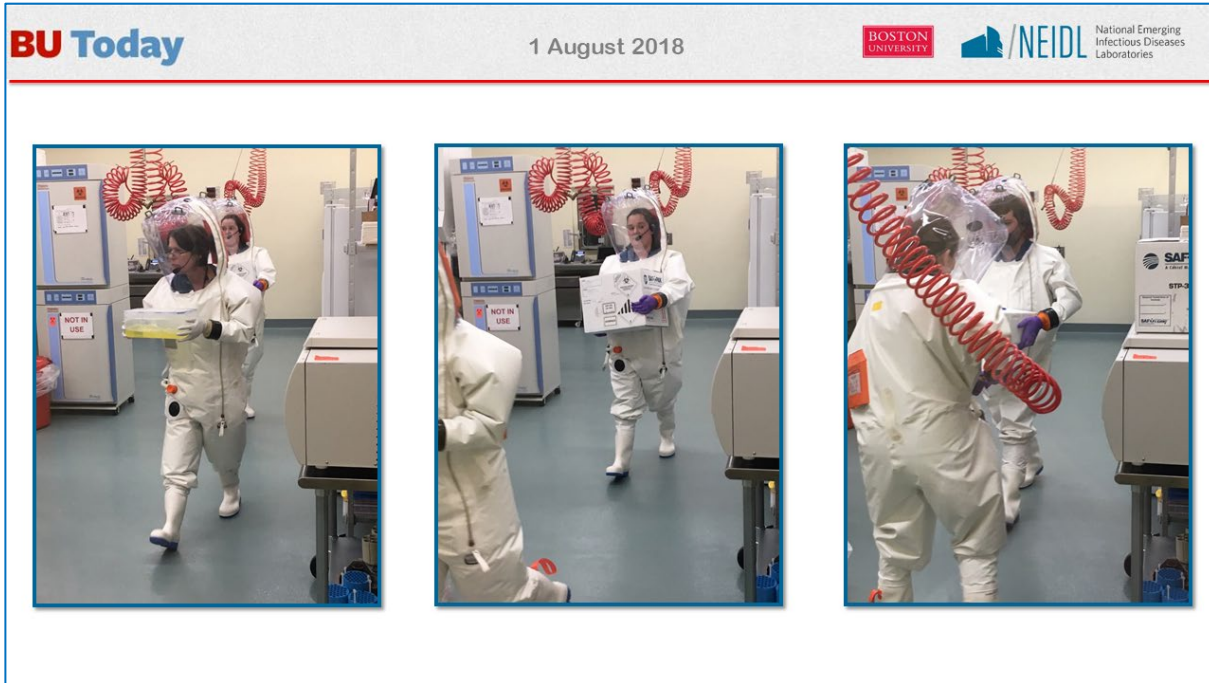
1. Perform innovative basic, translational and clinical research on emerging infectious diseases, especially those identified as high priority category A, B, and C agents (<http://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/cata.aspx>), in order to develop diagnostic tests, treatments and vaccines to promote the public's health.
2. Provide education and training in these areas of research, in order to develop the next generation of scientists in this field, and to support a national response in the event of a biodefense emergency.
3. Establish a research facility with the highest attention to community and laboratory safety and security.

To successfully implement and achieve these goals, NEIDL has developed and is implementing a strategic plan to:

1. Partner with academic departments across the university to recruit a cadre of investigators, as well as to develop research staff with expertise in the scientific disciplines required to investigate the pathogenesis of emerging infectious diseases caused by category A, B and C agents. We encourage and support the development of national and international research collaborations in order to carry out our mission.
2. Develop physiologically relevant models for the comparative study of these pathogens, mimicking as closely as possible the human disease process. Not only does this require that we recruit faculty with expertise in animal modeling and veterinarian pathology, but also develop the needed services to support these investigations.
3. Move promising basic research as rapidly as possible to translational, preclinical and clinical research in animals and humans in partnership with appropriate collaborators.
4. Create and establish the methodologies needed to advance the development and testing of vaccines, therapeutics and diagnostics for these agents.
5. Train scientists and related support personnel in the requirements to perform maximum containment research in a safe and secure environment.
6. Maintain the flexibility needed to support a national response in the event of a biodefense emergency.
7. Ensure a "safety first" environment for the conduct of all activities in the NEIDL

Highlights

The first Ebola sample arrives at the NEIDL



Notable Quotes

"This is clearly an important step for the NEIDL. This will permit us to fulfill our mission of studying emerging pathogens and developing diagnostics, therapeutics, and vaccines for these pathogens, even those that require BSL-4 containment. It has taken a very long time to get to this point, but the time that has passed has not dampened our enthusiasm—and excitement—to be able to start BSL-4 work."

"If you can't stop them (the pathogens) when the outbreak happens, then you're out in the position to try to play catch-up".

"This is exactly the place to have a facility like this," said Corley. "That allows us to get people who would not normally think about trying to solve these problems to get interested."

"Boston University's laboratory is one of only two Biosafety Level 4 labs in the country based at academic institutions, and the only one at a research-focused university. That means it offers opportunities to work across disciplines."

"We now have access to collaborators that would not normally think about working on pathogens: engineers, biostatisticians, people in fields such as regenerative medicine."

"I have learned that the only way to build trust is to be transparent and open and have open, respectful conversations even with the opponents."

Ronald B. Corley, Director NEIDL

"We are excited to use these cells because the liver is one of the main target organs of Ebola virus infection. We will use Gustavo's cells to find out why Ebola virus is so devastating for the liver."

"The lab is just so beautiful. I'm so excited to be here."

Elke Mühlberger, Associate Professor of Microbiology

"I intend to keep a close eye on things and I want to get to the Boston Public Health Commission to really make sure that they are going to be as transparent as they say they will be," he said.

Lynn Klotz, PhD, senior science fellow at the Center for Arms Control and Non-Proliferation

"Sure, these facilities have deadly diseases such Ebola, but you know what worries me more? Hospitals. "I see hospitals as bigger areas of risk if people really want to get ramped up about infectious disease threats (especially considering how they have acted as amplifiers for SARS and MERS, not to mention highly-resistant infections)."

"People don't work in BSL4 labs without a sense of awareness for the work they do—they are dedicated to the work and willing to risk their lives. It's not something they take lightly".

Saskia Popescu, MPH, MA, CIC, an infection prevention specialist and PhD candidate studying biodefense at George Mason University

FY19 BY THE NUMBERS

Faculty 22

Staff 123

Projects Funded 28

**Funds Awarded
\$25.5 Million**

Publications 60

**BSL-4 trained
faculty and staff 43**

- 8 Mentors
- 12 Independent access
- 14 Supervised access
- 9 In training

Facility Tours 16

Faculty and Staff

Scientific Leadership



Ronald B. Corley, PhD
Professor and Chair, Department of Microbiology
Director, NEIDL
Director, Immunology Core

Dr. Corley's Research interests:

- Innate and adaptive immunity to human pathogens



Gerald T. Keusch, MD
Professor of Medicine & International Health Associate
Director, NEIDL
Director, Collaborative Research Core

Dr. Keusch's research interests:

- Global impact of infectious diseases on economic development and public health

Faculty



Nahid Bhadelia, MD, MA
Assistant Professor, Medicine / ID
Medical Director, SPU, BMC

Dr. Bhadelia's research interests:

- International pandemics strategy and policy
- Healthcare worker training for disaster preparedness



Tonya Colpitts, PhD
Assistant Professor, Microbiology

Dr. Colpitts' research interests:

- Virus/Flavivirus pathogenesis
- Virus-host-vector interactions
- Transmission-blocking vaccines



John H. Connor, PhD
Associate Professor, Microbiology

Dr. Connor's research interests:

- Virus-host interaction
- Viral domination of protein synthesis
- Novel approaches to virus detection



Nicholas Crossland, DVM ACVP
Assistant Professor, Pathology

Dr. Crossland's research interests:

- *Borrelia burgdoferi* and mechanisms of persistence
- Comparative pathology using animal models



Robert Davey, PhD *
Professor, Microbiology

Dr. Davey's research interests:

- Host factor-based therapy development
- Infection mechanism for filoviruses



Florian Douam, PhD *
Assistant Professor, Microbiology

Dr. Douam's research interests:

- Viral immunogenicity and pathogenicity mechanisms in vivo
- Advanced humanized mouse systems



Paul Duprex, PhD *
 Director, Center for Vaccine Research
 University of Pittsburgh

Dr. Duplex's research interests:

- Paramyxovirus pathogenesis
- Virus-cell interactions
- Zoonosis; cross-species infection



Rachel Fearn, PhD
 Associate Professor, Microbiology

Dr. Fearn's research interests:

- Negative strand RNA virus polymerase activities
- Control of respiratory syncytial virus RNA synthesis



Horacio Frydman, PhD
 Associate Professor, Biology

Dr. Frydman's research interests:

- Niche tropism of insect endosymbionts
- Mechanisms of Wolbachia-insect interactions



James Galagan, PhD
 Associate Professor, Biomedical Engineering & Microbiology

Dr. Galagan's research interests:

- Mycobacterium tuberculosis regulatory networks
- Computational Biology and Genomics
-



Anthony Griffiths, PhD*
 Associate Professor, Microbiology

Dr. Griffiths' research interests:

- Multiple aspects of filovirus biology
- Development of vaccines and therapeutics



Tarik Haydar, PhD
 Assoc Professor, Anatomy & Neurobiology

Dr. Haydar's research interests:

- Forebrain development and function
 Cellular and molecular determinants influencing cognition



Thomas B Kepler, PhD
 Professor, Microbiology, Mathematics and Statistics

Dr. Kepler's research interests:

- Quantitative Systems Immunology
 Vaccine Development



Bang-Bon Koo, PhD
 Assistant Professor, Anatomy & Neurobiology

Dr. Koo's research interests:

- Biomedical in-vivo imaging
- Multimodal magnetic resonance imaging and analysis



Igor Kramnik, MD, PhD
 Associate Professor, Medicine and Microbiology

Dr. Kramnik's research interests:

- Genes controlling host resistance and susceptibility to TB
- Mechanisms of macrophage activation and differentiation

*Joined NEIDL in FY19

*Left NEIDL in FY19



Elke Mühlberger, PhD
Associate Professor, Microbiology
Director, Biomolecule Production Core

Dr. Mühlberger's research interests:

- Host response to filovirus infection
- Molecular mechanisms of filovirus replication and transcription



Jason Rock, PhD *
Associate Professor, Medicine
Principal Investigator, CReM

Dr. Rock's research interests:

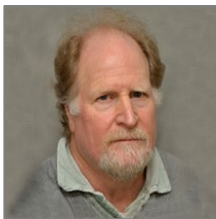
- Genetic, Molecular and Cellular therapies for the treatment of lung disease



Mohsan Saeed, PhD *
Assistant Professor, Biochemistry

Dr. Saeed's research interests:

- Role of viral proteases in shaping virus-host interactions



John C. Samuelson, MD, PhD
Professor of Molecular and Cell Biology
Professor of Microbiology

Dr. Samuelson's research interests:

- Pathogenesis of protozoan parasites
- Structures of parasite walls & glycoprotein



James Whitney, PhD *
Assistant Professor, Medicine, HMS
PI, Center for Virology and Vaccine Research, BIDMC

Dr. Whitney's research interests:

- Viral dynamics & the HIV-1/SIV viral reservoir
- Development of novel HIV-1 eradication strategies

Scientific Staff and Trainees

Agrahari, Garima *
Postdoctoral Fellow
Kramnik Lab

Anantpadma, Manu *
Sr. Research Scientist
Davey Lab

Araujo, Ricardo *
Visiting Scientist, MCTI Brazil
Colpitts Lab

Asad, Sultan **
Senior Research Scientist
Colpitts Lab

Avena, Laura *
Graduate Student, UTHS
Griffiths Lab

Baer, Cooper R
PhD Candidate, Microbiology
Galagan Lab

Braun, Molly
PhD Candidate, Microbiology
Fearn's Lab

Breen, Michael
PhD Candidate, Microbiology
Fearn's Lab

Broos-Caldwell, Aditi
Research Technician
NEIDL Repository

Brownhill, Eric

MD-PhD Candidate,
Microbiology
Kramnik Lab

Chatterjee, Sujoy
Postdoctoral Research
Associate
Kramnik Lab

Cressey, Tessa
PhD Candidate, Microbiology
Fearn's & Mühlberger Labs

Devaux, Alexander
Research Study Technician
Connor Lab

Donohue, Callie *
PhD Candidate, Microbiology

Davey Lab

Downs, Sierra *
Research Technician
Griffiths Lab

Dülsner-Seidel, Kirsten
Postdoctoral Fellow
Kramnik Lab

Feitosa-Suntheimer, Fabiana
ACL3 Insectary Manager
Colpitts Lab

Fofana, Josianne
PhD Candidate, Microbiology
Mühlberger Lab

Gavrish, Igor
Research Study Technician
Kramnik Lab

Gold, Alexander
PHD Candidate, Microbiology
Colpitts Lab

Hayward, Oliver **
PhD Candidate, Microbiology
Fearn Lab

He, Xianbao
Research Instructor
Kramnik Lab

Ho, Gregory
Research Technician
Duprex Lab

Hume, Adam J
Research Scientist
Mühlberger Lab

Johnson, Rebecca *
Postdoctoral Fellow
Griffiths Lab

Kleiner, Victoria
PhD Candidate, Microbiology
Fearn Lab

Keiser, Patrick *
Senior Research Technician
Davey Lab

Koster, Jacob
Sr. NEIDL Core Technologist
Quality Control

Ludeke, Barbara
Postdoctoral Fellow
Fearn Lab

Malsick, Lauren

Undergraduate Student,
Biology
Fearn Lab

Mameli, Enzo *
Visiting Researcher, HSPH
Colpitts Lab

Manhart, Whitney
PhD Candidate, Microbiology
Mostoslavsky Lab

Marquette, Meghan *
Visiting Researcher, MIT
Colpitts Lab

McKay, Lindsay *
Postdoctoral Fellow
Griffiths Lab

Mori, Hiroyuki *
Postdoctoral Fellow
Davey Lab

Murphy, Linda J.
Senior Research Scientist
Duprex Lab

**Nambulli, Shamkumar
(Sham) ***
Research Scientist
Duprex Lab

Odom, Christine
PhD Candidate, Microbiology
Connor Lab *

Olejnik, Judith
Senior Research Scientist
Mühlberger Lab

Olsen, Michelle T. **
Postdoctoral Fellow
Connor Lab

Pacheco, Jennifer R.
Research Technician
Mühlberger Lab

Philip, Katherine *
Undergrad Student, Biology
Fearn Lab

Ruedas, John *
Postdoctoral Fellow
Connor Lab

Shafik, Andrew *
Postdoctoral Fellow
Connor Lab

Shareef, Afzaal
Research Study Technician
Fearn Lab

Shearer, Sarah
Senior Research Scientist
Fearn Lab

Soucy, Alexandra *
Research Study Technician
Connor Lab

Storm, Nadia *
Postdoctoral Fellow
Griffiths Lab

Strampe, Jamie
Graduate Student,
Bioinformatics
Connor Lab

Suder, Ellen Lee
PhD Candidate, Microbiology
Colpitts Lab

Tilston-Lunel, Natasha *
Postdoctoral Fellow
Duprex Lab

Waligurski, Emily
Research Study Technician
Kramnik Lab

Yen, Judy
Sr. NEIDL Core Technologist
BSL4 Operations

Yabaji, Shivraj *
Postdoctoral Fellow
Kramnik Lab

*Joined NEIDL in FY19
*Left NEIDL in FY19

Animal Research Support

Diaz-Perez, Yulianela
Veterinary Research Tech

Furtado, Oscar M
Veterinary Research Tech

Gross, Sarah
Veterinary Research Tech

Grosz, Kyle *
Veterinary Research Tech

**Hardcastle, Kath DVM
DACLAM**
ABSL-4 Core Director, ASC

Harrington, Patrice
Veterinary Research Tech

Nunes, Corey
Operations Manager,
NEIDL ASC

MacGregor, Nicolle
Veterinary Research Tech

Mclaughlin, Robert J
Veterinary Research Tech

Varada, Rao DVM PhD
Attending Veterinarian, ASC

Operations Leadership



Ronald B Corley, PhD
Director, Administration



Thomas Daley
Director, Operations



Kevin Tuohey
Interim Chief Safety Officer

Administration

Durkop, Betina A
Executive Coordinator

Forman, Lora
Administrative Manager,
Operations

Spell, Virginia *
Research Contracts Manager

Trevino, Richard , MPH
Director, Finance & Research Administration

Community Relations

Britton, Valeda J JD
Executive Director, Community Relations
Boston University Government Affairs

Idiokitas, Chimel
Assistant Director, Community Relations
Boston University Government Affairs

Facilities Maintenance & Operations

Amadio, Paul
Facilities Engineering Ops
Manager

Ananian, David
General Mechanic

Baires, J Victoria
Custodian

Bolger, Eileen **
Control Center Tech I

Corbett, Joseph
Controls Manager

Fonseca, Paulo *
Control Technician I

Gendron, Jonathan
General Mechanic

Kjersgard, Eric
Control Center Tech II

Morahan, Richard *
Mechanic

Mosca, Derek
Maintenance Mechanic

Munroe, James *
General Mechanic

Murphy, James **
General Mechanic

Rodriguez, Mario
Custodian

Rusk, Scott
Director, Facilities &
Maintenance Operations

Sousa, Daniel
Shipping & Receiving

Tucker, Daniel
Maintenance Mechanic

Tupe, Michael
Maintenance Mechanic

Walsh, James **
General Mechanic

Information Technology

John McCall
Director of IT

Benjamin Slutzky
IT Administrator

Environmental Health & Safety

Benjamin, Shannon MBA
CBSA
Associate Director, Research
Safety for High Containment

Ellis, Andrew W *
Sr. Research Safety Specialist

Flynn, Nick *
Biocontainment Operations
Manager

Gilmartin, John *
EHS Program Manager

Madico, Guillermo MD PhD
Scientific Safety Officer

Olinger, Gene PhD
Associate Director, Maximum
Containment Training

Tuohey, Kevin M
Interim CSO; Exec. Director
Research Compliance

Vinson, Aron J
Program Manager, Emergency
Response Planning

Yun, Nadezhda, MD
Associate Director, Research
Safety for Maximum
Containment

Research Occupational Safety

Thomas Winters, MD
Medical Director, Research
Occupational Health Program

Nahid Bhadelia, MD, MA
Assistant Professor, Medicine / ID
Medical Director, Special Pathogens Unit
Boston Medical Center

Public Safety

Management & Staff

Gibbons, William *

Director, Public Safety, BUMC

Paparo, Scott

Systems Integrator

Puleo, Matthew R

Systems Integrator

Taranto, Stephen L *

Director of Public Safety BUMC

Tracy, Harris

Systems Integrator

Zarth, Melody L *

Personnel Suitability Specialist

Public Safety Officers

Annese, Rae

Barros, Christopher L

Barros, Jeffrey P

Duffy, Joseph M

Gallivan, John

Granados, David J

Maldonis, Joseph

O'Hara, Sean R

Phelps, Justin

Saad, Jacob

Salhi, Adil

Spellman, David F

Tupe, Michael T

Wynne, Paul M

Wynne, Sean C

*Joined NEIDL in FY19

*Left NEIDL in FY19

Research Publications

Olsen ME, Cressey TN, Mühlberger E, **Connor J.H.** (2018) Differential Mechanisms for the Involvement of Polyamines and Hypusinated eIF5A in Ebola Virus Gene Expression. *J Virol.* 2018 Jul 25. pii: JVI.01260-18. doi: 10.1128/JVI.01260-18. PMID: 30045993

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A St. Blanc, **NA Crossland**, PM DiGeronimo, RE Cianciolo, GJ Pirie, AE Thiessen, N Wakamatsu. Urothelial carcinoma of the urinary bladder resulting in persistent uroabdomen with concurrent lipogranulomatous tubulointerstitial nephritis in an adult intact female Serval (*Leptailurus serval*). *JAVMA.* 2018. PMID: **29911950**.

NA Crossland, P DiGeronimo, J Wellehan, Y Sokolova, A Childress, J Nevarez, D Paulsen. Pneumonia in a captive central bearded dragon (*Pogona vitticeps*) with concurrent detection of Helodermatid adenovirus 2 and a novel mycoplasma species (*Mycoplasma pogona*): clinical, histological, ultrastructural, and molecular findings. *Vet Path.* 2018. PMID: **29940815**

NA Crossland, P Viadanna, T Waltzek, J Hawke, F Del Piero. Investigation of a Cyprinid herpesvirus-1 disease episode in a group of pond-reared koi. *JAAH.* 2018. PMID: 29672928.

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Cui Q, Cheng H, Xiong R, Zhang G, Ruikun Du, Anantpadma M, **Davey RA** and Lijun Rong Identification of Diaryl-Quinoline Compounds as Entry Inhibitors of Ebola Virus. *Viruses* 2018, 10(12), 678; <https://doi.org/10.3390/v10120678>.

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FY19 Funded Research

The work which resulted in the publications outlined above would not have been possible without the ability of our faculty to competitively seek funding to support their research activities. NEIDL faculty members received over \$ 25 Million in funding in FY19 for the following projects:

School/Dept	PI	GRANT	SPONSOR	PROJECT PERIOD	FUNDED IN FY19
NEIDL FACULTY AWARDS					
BUSM/MED-ID	NAHID BHADELIA	CUPID: CONTEXT-AWARE UNOBSTRUCTIVE PREDICTION OF INDICATORS FOR DIAGNOSIS OF HEALTH RISKS	DOD/DARPA - UTRC	4/15/18-12/15/21	55,400
BUSM/MICRO	TONYA COLPITTS	EFFECTS OF PRE-EXISTING DENGUE VIRUS IMMUNITY ON ZIKA VIRUS INFECTION	NIH/NIAID	8/7/17-7/31/19	206,250
BUSM/MICRO	JOHN CONNOR	SBIR PHASE II: HIGH-THROUGHPUT AND SCALABLE NANOPARTICLE CHARACTERIZN FOR LIFE SCIENCES	NSF - Nanoview Diagnostics Inc.	8/15/18-7/31/20	100,000
BUSM/MICRO	JOHN CONNOR	GENETIC PROBING OF RESIDUES INVOLVED IN EBOV GLYCOPROTEIN	NIH/NIAID	7/1/18-6/30/20	206,250
BU/NEIDL	RON CORLEY	NATIONAL EMERGING INFECTIOUS DISEASES LABORATORIES OPERATIONS	NIH/NIAID	6/1/16-5/31/21	11,500,000
BUSM/MICRO	ROB DAVEY	STRUCTURAL AND FUNCTIONAL CHARACTERIZATION OF THE EBOLA VIRUS REPLICATION COMPLEX	NIH/NIAID - The Washington Univ	7/1/18-6/30/21	292,000
BUSM/MICRO	ROB DAVEY	SMALL MOLECULE INHIBITORS OF EBOLA VIRUS POLYMERASE FUNCTION	NIH/NIAID - GSU	8/1/18-1/31/20	316,764
BUSM/MICRO	ROB DAVEY	EMERGING VIRUS-HOST CELL PROTEIN INTERACTION NETWORKS	NIH/NIAID - Purdue University	8/1/18-3/31/20	533,510
BUSM/MICRO	ROB DAVEY	MODELING FILOVIRUS INFECTION OF AND TRAFFICKING THROUGH SKIN	NIH/NIAID - The University of Iowa	8/1/18-7/31/19	288,750

School/Dept	PI	GRANT	SPONSOR	PROJECT PERIOD	FUNDED IN FY19
NEIDL FACULTY AWARDS					
BUSM/MICRO	RACHEL FEARNS	DEVELOPING COMBINATION THERAPIES AGAINST PNEUMO- &PARAMYXOVIRUSES CAUSING SEVERE RESPIRATORY INFEC	NIH/NIAID - GSU	7/1/18 - 6/30/19	16,500
BUSM/MICRO	RACHEL FEARNS	MECHANISMS OF MARBURG VIRUS GENE EXPRESSION	NIH/NIAID	5/8/18 - 4/30/23	529,282
BUSM/MICRO	RACHEL FEARNS	MECHANISM OF ACTION OF AN RSV N PROTEIN INHIBITOR	Enanta Pharm, Inc	4/1/18 - 10/15/19	84,560
BUSM/MICRO	RACHEL FEARNS	EVALUATING THE MECHANISM OF ACTINO OF RSV L INHIBITORS TARGETING THE CRV REGION	Janssen Sciences Ireland	5/3/19 - 5/2/20	137,860
ENG/BME	JAMES GALAGAN	DEVELOPMENT OF A WEARABLE PHYSIOLOGICAL STATUS MONITOR	The Jackson Fdn / Uniformed Servs U	9/25/18 - 9/24/21	2,335,996
BUSM/MICRO	ANTHONY GRIFFITHS	CHARACTERIZATION OF THE DISEASE COURSE IN RHESUS MACAQUES INFECTED WITH EBOLA VIRUS	HHS/ASPR/B ARDA MRI Global	11/13/18 - 7/12/20	1,354,230
BUSM/MED	IGOR KRAMNIK	NECROSIS IN PULMONARY TB GRANULOMAS: DYNAMICS, MECHANISMS, THERAPIES	NIH/NHLBI	5/1/16 - 4/30/20	716,257
BUSM/MED	IGOR KRAMNIK	ABERRANT IMMUNE ACTIVATION IN THE TUBERCULOUS GRANULOMA: A PIVOTAL ROLE IN NECROSIS	NIH/NHLBI	7/15/16 - 6/30/20	1,477,256
BUSM/MICRO	ELKE MUHLBERGER	DECIPHERING THE PATHOGENIC POTENTIAL OF LLOVIU VIRUS, A NOVEL FILOVIRUS	NIH/NIAID	2/13/18 - 1/31/20	247,500
BUSM/MICRO	ELKE MUHLBERGER	THE ROLE OF TLR4 SIGNALING IN THE PATHOGENESIS OF FILOVIRUS INFECTION	NIH/NIAID	5/10/18 - 4/30/20	206,250
					\$ 20,604,615

School/Dept	PI	GRANT	SPONSOR	PROJECT PERIOD	FUNDED IN FY19
AFFILIATED FACULTY GRANTS					
BUSM/MICRO	TOM KEPLER	CHAVI-SRSC J COMPUTATIONAL BIOLOGY	NIH/NIAID Duke U	7/15/12 - 6/30/19	204,625
BUSM/MICRO	TOM KEPLER	STRUCTURE-FUNCTION ANALYSIS OF INFECTION- AND VACCINE-INDUCED B-CELL REPERTOIRES	NIH/NIAID Children's Hosp	8/1/2017-7/31/22	87,000
BUSM/MICRO	TOM KEPLER	HIV-1 VACCINE-ELICITED ANTIBODS TARGET ENVELOPE GLYCANS	NIH/NIAID Duke U	6/1/18 - 5/31/19	18,071
BUSM/MICRO	TOM KEPLER	NEISSERIAL PORINS AND ANTIGEN PRESENTING CELLS	NIH/NIAID Boston Medical Ctr	9/1/16 - 8/31/19	134,327
BUSM/MICRO	TOM KEPLER	MODELING AFFINITY MATURATION AT MOLECULAR RESOLUTION	NIH/NIAID	4/15/15 - 3/31/20	2,508,462
BUSM/MICRO	TOM KEPLER	THE B CELL REPERTOIRE AS A WINDOW INTO NATURE & IMPACT OF LUNG VIROME	NIH/NHLBI	5/1/19 - 4/30/22	832,073
BUSM/MICRO	TOM KEPLER	STRUCTURE BASED DESIGN OF ANTIBODIES AND VACCINES	NIH/NIAID VUMC	5/1/19 - 4/30/20	78,500
BUSM/ANAT	TARIK HAYDAR	HETEROGENEITY OF FOREBRAIN NEURAL PRECURSORS	NIH/NIND	9/30/15 - 6/30/20	674,322
BUSDM / MOL & C BIO	JOHN SAMUELSON	STRUCTURE AND DEVELOPMENT OF OOCYST AND SPOROCYST WALLS	NIH/NIAID	8/1/15 - 1/31/20	408,250
					\$ 4,945,630
Total Grants					\$ 25,550,245

NEIDL Faculty and Staff Recognition

An indication of the reputation of faculty is best exemplified by their selection as invited speakers in national and international forums, service on review panels and service on editorial boards of journals. Other forms of recognition include being sought after because of their experience and ability to use their expertise to explain a story to the news media about current events. NEIDL faculty continue to be recognized as summarized below.

Editorial Boards

Connor

Journal of Virology

Duprex

Board of Editors, MSphere
Editorial board, J. Gen. Virology

Fearns

Invited guest editor, PLOS Pathogens, 2018

Griffiths

Frontiers in RNA

Koo

Reviewer, Frontiers in Neuroanatomy
Reviewer, Journal of Comparative Neurology

Invited lectures (national and international)

Connor

UC Irvine, Irvine CA. January 2019
Mayo Clinic, Rochester MN. March 2019
Photonics West San Francisco (keynote speaker),
February 2019
Ebola virus Is Addicted to Polyamines and Hypusinated
eIF5A. Gordon Research Conference on polyamines, June
2019

Colpitts

“Discovery of arbovirus transmission factors”, Tulane
University School of Public Health & Tropical
Medicine/New Orleans Mosquito, Termite & Rodent
Control Board, New Orleans, LA. November 2018

Crossland

Use of Recombinant Fluorescent Viruses to Study the
Pathogenesis of Measles Virus, Rocky Mountain
Laboratories (NIAID), Use of Laboratory Animals in
Infectious Disease Research. August 2018
Digital Pathology Halo Image Analysis, Annual ACVP
meeting. October 2018
Mystery Slide #2: Measles Associated Lymphoid
Depletion, Important Non-Human Primate Viral
Pathogens, Washington D.C. ACVP Pre-Meeting
Workshop Primate Pathology. November 2018

Davey

Ebola virus entry mechanism and treatment. University
of Alabama, Birmingham. October 2018
Exploiting Ebola virus infection mechanism for therapy
development. The 17th Awaji forum on Infection and
Immunity. March 2019.

Fearns

Chairperson, Expressing and Multiplying Session,
Negative Strand Viruses Conference, Verona, Italy,

July 2018.

University of Kentucky, Department of Molecular and
Cellular Biochemistry, Lexington, KY, USA. October, 2018
University of Pennsylvania, Department of Microbiology,
Philadelphia PA, USA. October 2018
Plenary Speaker, RespiDART 2018 Conference, Miami FL,
USA. November 2018
Emerging and Re-emerging viruses conference, Tofo,
Mozambique. September 2018

Griffiths

Co-Chair American Society for Microbiology Biothreats
Meeting, Washington DC. February 2019
NIH/DoD Filovirus Animal Non-Clinical Group (FANG),
Bethesda, MD. “Comparison of EBOV-vaccine efficacy in
IM- and IN-challenged cynomolgus macaques.” May 2019

Hardcastle

ABSL3 biological sample movement. American Biological
Safety Association (ABSA) Annual Conference,
Cambridge, MA. September 2019

Kepler

Jilin University: AIDS and Vaccine, Changchun, China.
September 2018
Immunology Departmental Seminar, University of
Toronto, Toronto, Ontario. January 2019
Center for Cell Analysis and Modeling Seminar,
Connecticut Health Sciences Center. June 2019

Kramnik

Hyperinflammation and immune suppression in TB
susceptibility – two sides of the same coin? BU Dental
School seminar October 30, 2018
Multigenic control of host susceptibility to pulmonary
TB. The Many Hosts of Mycobacteria 8th Meeting. Albert
Einstein College of Medicine. Bronx, NY. March 4-6, 2019
Workshop organizer “Mouse models of tuberculosis”.
The Many Hosts of Mycobacteria 8th Meeting. Albert
Einstein College of Medicine. Bronx, NY. March 6, 2019
Host-Pathogen Interactions in TB: Collision or Collusion?
NIH Intramural TB Research Initiative. April 1, 2019

Mühlberger

How to work with Ebola virus without a BSL4 lab.
Department of Microbiology and Immunology, University
of Texas Medical Branch, Galveston, TX. October 16,
2018.

Rock

Gordon Conference on Tissue Niches and Resident Stem
Cells in Adult Epithelia [*Invited Lecture and Session
Chair*], August 2018
University of Alabama, Birmingham, Pulmonary Division
[*Invited Lecture*], 2018

American Thoracic Society International Conference, Dallas, TX [*Science Innovation Center, Invited Speaker*], May 2018
Fusion Conference on Epithelial-Mesenchymal Interactions in Lung Development and Fibrosis [*Invited Lecture*], February, 2019

Memberships

Hardcastle

Elected member of the ACLAM National Mock Exam Committee

Griffiths

International Committee on the Taxonomy of Viruses (ICTV) *Filoviridae* study group (Member)

Kepler

Society for the Social Study of Science, February 2019
History of Science Society, 2018-Present
Philosophy of Science Association, -Present

Koo

Member of International Neuropsychological Society
Member of International Brain Injury Association

NIH Study Sections and Review Panels

Connor

Reviewer Zika R21 study section
Reviewer F31/32/30 fellowship study section
Reviewer NIAID review panel Virology A
Reviewer NIAID review panel Virology A
Reviewer NIAID review panel SEP (conflict of interest panel)

Colpitts

Reviewer for National Institutes of Health, NIAID R13 panel
Scientist Reviewer for US DOD MIDRP Military Medical Research panel
Scientist Reviewer for US DOD PRMRP Viral Infectious Diseases panel
Scientist Reviewer for US DOD PRMRP Vaccine Development Discovery panel
Scientist Reviewer for US DOD PRMRP Infectious Disease panel
Scientist Reviewer for US DOD MIDRP Flavivirus: Dengue Vaccine panel
National Science Foundation PMB CAREER Panel Reviewer
Reviewer for Kansas City Area Life Sciences Institute Nexus Competition

Fearns

Ad Hoc grant reviewer for the French National Research Agency, 2018
CSR reviewer for study titled "Program Evaluation of NIH Peer Review Processes: The Role of Anonymization, 2018
Member NIH Special Emphasis Panel, Non-coding RNAs, 2019

Member Ad Hoc NIH Virology B study section, 2019
Member NIH Virology B study section, 2019-2023

Griffiths

NIH study section Non-HIV microbial vaccine development NIH ZRG1 IMM R12. November 2018
NIH study section Non-HIV microbial vaccine development NIH ZRG1 IMM R12. March 2019
NIH study section Non-HIV microbial vaccine development NIH ZRG1 IMM R12. June 2019
DoD PRMRP Discovery ID-2. June 2019
NIH study section 2019/10 ZRG1 IMM-R (50) R RFA-AI-18-054 U.S.-Brazil Collaborative Biomedical Research Program. July 2019

Kepler

CSR VACC Member, July 2018
NIAID ZAI1-JA-I-C1 Chair, February 2019
NIAID ZAI1-PTM-I-M1 Member, March 2019

Kramnik

Special Emphasis Panel "Molecular Landscape of Aging Lung" (RFA HL-19-012) July 2018
Special Emphasis Panel ZRG1 AARR M 57 "Mechanisms of Mycobacterial-Induced Immunity in HIV-Infected and Uninfected Individuals to Inform Innovative Tuberculosis Vaccine Design ". March 2019

Mühlberger

NIH Study section Virology-A (VIRA), October 22-23, 2018
German Research Council, Evaluation of the Institute of Microbiology of the German Army, Germany, April 4-5 2019
Medical Research Council (MRC), UK 2019NIH Member of Study section Virology-A (VIRA) 2019 – 2023

Rock

Impact of Microenvironment on Lung Progenitor Cell Function, 2018
Molecular Atlas of Lung Development Program (LungMAP) Phase 2, 2019
2018 Ontario Institute for Regenerative Medicine
2019 American Institute of Biological Sciences/Flight Attendant Medical Research Institute, Centers of Excellence

Samuelson

Ad Hoc Reviewer for NIH Special Emphasis Panel in January 2019

Patents

Title: Inhibitors of Macropinocytosis in Prevention and Treatment of Disease
U.S. patent No. 10,111,881, 2018. **Davey RA** and Anantpadma M.

Title: ROCAGLATE COMPOUNDS AND USES THEREOF
U.S. Provisional Application No.: 62/863,471
Filed: June 19, 2019, **Kramnik, Igor et al.** BU Ref. No.: 2019-039. NP Ref. No.: 701586-095630PL01

Introducing New Faculty

Robert A. Davey, PhD

Dr. Robert Davey, PhD joined Boston University in August 2018, as a Professor of Microbiology. He received his doctorate in Microbiology and Immunology at the University of Adelaide in Australia and continued his training as a Postdoctoral Fellow at the Howard Hughes Medical Institute and then at the Division of Hematology, both with Dr. James Cunningham at Brigham and Women's Hospital and Harvard Medical School.

Dr. Davey comes from Texas Biomedical Research Institute, where he was a Ewing Halsell Scholar and Scientist at the Department of Virology and Immunology. While there, his work was focused on identification of cellular factors important for establishing infection by filovirus and bunyaviruses, culminating in a deeper understanding of the entry and cell signaling pathways that are used by these viruses to penetrate the cell membrane and establish infection.

One of the major viruses he now focuses his laboratory on is that of Ebola virus. He is one of a handful of investigators who are well known for their work on the cell biology of filovirus infection. While he uses pseudotyped viruses for some of his studies, he has focused on elucidating Ebola virus entry mechanisms using authentic Ebola virus under BSL-4 conditions.

Florian Douam, PhD

Dr. Douam joined the NEIDL faculty as an Assistant Professor of Microbiology on July 01, 2019. He had just completed an especially productive postdoctoral fellowship with Alexander Ploss at Princeton. While there, he developed innovative "humanized mouse" models to study host responses to emerging viruses. This new mouse model offers unprecedented opportunities for better understanding the molecular mechanisms governing flavivirus pathogenesis and immune responses in a human context. His translational approaches lend themselves not only to studying viral pathogenesis, but will also serve to help screen for therapeutics to help protect against emerging viruses. His studies also provide insight into what makes a vaccine a good vaccine, remarkably, something science has yet to decipher.

Dr. Douam has received a number of awards for his research. Most recently, he was awarded the NIH K22 career transition award with the highest priority score possible. His work has been published in outstanding journals including PLoS Pathogens, mBIO, Proc. Natl. Acad. Sci., and Nature Communications among them.

Anthony Griffiths, PhD

Dr. Anthony Griffiths joined the NEIDL faculty as an Associate Professor of Microbiology in September 2018. Dr. Griffiths got his Ph.D. from the University of Reading and completed his postdoctoral research training in Dr. Don Coen's laboratory at Harvard Medical School, where he studied various aspects of the molecular biology of DNA viruses, work he continued to pursue after moving to Texas Biomedical Research Institute in 2006. It was during this time that he defined for the first time a frameshift mutation that led to drug resistance, and further demonstrated that these viruses generate microRNAs, some of which are incorporated into virions.

Dr. Griffiths' program evolved as he began to incorporate research on Ebola virus pathogenesis, which now forms the basis for the work he is conducting at Boston University and the NEIDL. Given his track record in virology, it is not surprising that Dr. Griffiths has already made important contributions to the Ebola virus field. Rather than approaching animal studies using the same parameters as most other laboratories (injection model), he took a different tactic. Instead, he developed an intranasal mucosal infection model, one that may best mimic human disease.

Dr. Griffiths has developed a solid funding record since moving to Texas Biomedical Research Institute. His funding supports in vivo studies on vaccines and therapeutics, and he will bring those experiences in building his program at Boston University. Importantly, he has developed a good laboratory practice (GLP) program at

his current institution, a program that is essential for preclinical testing and support from BARDA, as well as for contracts from DMID at NIH. Anthony is now working on establishing this program in the NEIDL.

Mohsan Saeed, PhD

Dr. Mohsan Saeed, PhD joined Boston University in March 2019 as an Assistant Professor of Biochemistry. With a background in veterinary medicine and microbiology, Dr Saeed went on to pursue graduate studies with Professor Wakita at the University of Tokyo, Japan where he earned his PhD in Pathology, Immunology and Microbiology. Dr. Saeed then carried out postdoctoral work in the laboratory of Dr. Charles M. Rice at Rockefeller University, in New York. Dr. Saeed's postdoctoral research involved two projects, both focused on development of cell-based HCV replication systems, which are essential for virtually any study of HCV biology and for the identification of anti-viral therapies. These efforts resulted in an impressive collection of eight publications, including a groundbreaking *Nature* paper, of which he was the first author, solving a 25-year old mystery of why patient-derived HCV does not grow in cell culture, and providing a platform to study diverse aspects of HCV biology and develop novel antiviral strategies.

As an independent investigator at Boston University, Dr. Saeed is now focusing on a novel biochemical approach to understanding viral infection, which he developed entirely on his own in Dr. Rice's lab. This approach involves a creative application of unbiased proteomics to identify and characterize the set of proteins cleaved during diverse viral infections (the viral "degradome"). Initially he is focusing his efforts on functional characterization of the novel cleavage events he has already identified for a few picornaviruses, with a special focus on emerging and reemerging enteroviruses of clinical importance. He is then planning to expand his work to analyze the degradomes of arboviruses in their insect vectors and vertebrate hosts. Arboviruses are a diverse group of pathogenic viruses that replicate in both vertebrates and arthropods, including emerging viruses such as dengue, yellow fever, and Zika.

Featured NEIDL Research

The batty, explosive history of bats in the military — and why this new idea just might work



A colony of approximately 1.5 million Mexican free-tailed bats swoops out from its home under Austin's Congress Avenue Bridge in 2005. (Jeff Haynes/AFP/Getty Images)

Original Article from The Washington Post By Lucy Cooke. July 2, 2018

The U.S. military has a long history of enlisting the help of animals in warfare. The bottlenose dolphin's sophisticated bio sonar enabled the Navy to detect and clear underwater bombs during the Iraq War, and homing pigeons played a vital role as secret messengers during both world wars, with some awarded medals for bravery.

But there is one animal that the military has had significantly less success in conscripting, and that is the bat.

In the wake of the Pearl Harbor bombing in 1941, hundreds of Mexican free-tailed bats were recruited as part of a harebrained scheme to blow up Japanese cities by arming the flying insectivores with bombs and releasing them from planes. The idea was that the bats would roost in buildings and explode, killing the enemy as they slept. What could possibly go wrong?

Well, quite a lot. The plot was riddled with flaws. No one had invented a bomb smaller than a can of beans, which would be impossible for an animal the size of a mouse to carry. And, most crucially, bats — unlike dolphins and pigeons — cannot be trained to follow orders.

Despite its imperfections, the batty plot was nevertheless given the green light. Its creator, a maverick Pennsylvania dentist and inventor named Lytle Adams, had some friends in high places. He had persuaded first lady Eleanor Roosevelt to check out one of his earlier ideas — a plane that delivered mail without landing. So when he detailed the bat proposal in a letter to President Franklin D. Roosevelt, it didn't immediately wind up in the trash. Instead, it was forwarded to the National Research Defense Committee — the group from which the Manhattan Project was spun off — with a presidential note of recommendation.

"This man is not a nut," Roosevelt wrote. "It sounds like a perfectly wild idea but is worth looking into."

The bat bomb plan was stamped “top secret” and assigned the suitably sci-fi code name Project X-Ray. A crack team of senior Army types, arsenal experts, engineers and biologists was assembled. Together, they set about vaulting the scheme’s more vertiginous hurdles.

The first stage was to capture thousands of Mexican free-tailed bats from caves in the Southwest, where they roosted in the tens of millions. Then a bomb had to be developed that was light enough for half-ounce bats to transport. In a quintessentially American twist, parts for the diminutive bomb were manufactured in a factory owned by crooner Bing Crosby.

With bats and bombs sorted, it was time to conjoin them. The miniature explosives were to be attached to the bats with twine, the presumption being that the bats would gnaw through it and leave the bombs behind. Then came the issue of controlling the bats. They were placed in refrigerators, forcing them into torpor for easy handling and transportation. But timing their thaw proved tricky. Several early tests with dummy bombs were a dud because the bats woke too late (causing them to plummet ingloriously to the ground once released) or too soon (before their cargo had been attached and allowing them to escape the base).

Undeterred, the scientists ran a test using real incendiary devices in June 1943. Things did not go as planned. A report on the experiment stated somewhat evasively that “testing was concluded . . . when a fire destroyed a large portion of the test material.” It failed to mention that the barracks, control tower and several other buildings at the auxiliary field station in Carlsbad, N.M., were set spectacularly ablaze by escapee bat bombers. The need to maintain military secrecy prevented civilian firefighters from entering the scene, and fire leaped from building to building, incinerating most of the base. As a final insult, a couple of winged missiles went AWOL, taking up roost under a general’s car before exploding.

The project never recovered from this ignominious retreat, and it was canceled in 1944. Having set up some 30 tests and spending a couple million dollars, the United States put its focus behind developing a bomb that exploited the power of atoms. This proved to be easier to control than bats.

Today, the U.S. military is again interested in bats not as front-line attackers but as defenders against a potentially devastating threat: Russian bioweapons.

Fruit bats have an almost supernatural ability to harbor some of the planet’s most deadly viruses without getting sick themselves. Inject an Egyptian fruit bat with the Marburg virus — a hemorrhagic relative of the infamous Ebola virus — and nothing happens. Do the same thing to a human, and within a week, the patient could be bleeding to death.

These bats’ extraordinary super-immunity has long fascinated virologists, and new research has shed light on how these flying frugivores achieve their supreme skill. Unpacking the mystery involved some cunning detective work from a coalition of scientists at Boston University and the U.S. Army Medical Research Institute of Infectious Diseases. Their work was published in the journal *Cell*.

An Egyptian fruit bat in an abandoned quarry on the Mediterranean island of Cyprus in 2007. (Alex Mita/AFP/Getty Images)



“What we are trying to do is to study bat immunology, but that turned out to be a very difficult thing to do when starting from scratch,” said **Thomas Kepler**, a professor of microbiology at Boston University. It took decades to create the reactive substances necessary to study human or mouse antibodies. With bats, he explained, they were starting from zero.

So **Kepler**’s team jump-started its work by examining the whole genome of the Egyptian fruit bat, chosen because it is a known reservoir for the lethal Marburg virus. It took two years just to assemble the genome. Once done, they compared it with other mammals’ genomes to hunt for idiosyncrasies, in particular an increase in size in any gene families that control the production of defensive proteins involved with immunity. They found significantly large interferon genes.

“These are interesting and very important, as they serve as the front line of anti-viral defense,” **Kepler** said. Once a cell has become infected by a virus, the interferons alert the surrounding cells. “They are basically a warning saying, ‘I’ve just been infected,’ ” he said. Neighboring cells then start shoring themselves up for a viral invasion.

The other supersize set of genes in the fruit bat controlled the receptors on “natural killer,” or NK, cells. These are essentially the body’s police system for identifying infected cells. Typically, these receptors are activating,

which means they trigger the NK cell to kill the damaged cell. But the fruit bat's NK receptor genes appear to activate and inhibit NK cell function.

This suggested to **Kepler** and his team that the bat immune system may respond in a unique way to viral infection, offering what he calls "soft protection." Instead of attacking and killing an infected cell, which leads to a cascade of inflammatory responses in the host, their NK cells might have a more nuanced response. They might, for instance, effectively starve the virus by turning down the host's cellular metabolism.

The bat's unique approach to viral infection could also explain why viruses that transfer from bats to humans, including Ebola, are so severe. "A virus that has co-evolved with the bat's anti-viral system is completely out of its element in the human," **Kepler** said. "That's why it is so deadly — the human immune system is overwhelmed by the inflammatory response."

Kepler believes that this insight into the fruit bat's super-immunity could eventually lead to a cure for Marburg. "It's possible that we could develop drugs that dampen down inflammation and arrest the virus by depriving it of what it needs to grow rather than trying to kill it outright," he said.

So where do bioweapons come in? Natural outbreaks of Marburg virus infection have occurred in African countries and are rare but extremely deadly, with a fatality rate of up to 90 percent. There is no antidote — and that has made the Marburg virus a prime candidate for biological warfare.

The Soviets had a keen interest in the Marburg virus in the 1980s and managed to develop an especially lethal strain after an accident at the Vector Institute, their germ warfare center in Siberia. The chief scientist there, Nikolai Ustinov, accidentally injected his thumb with the virus, which was intended for a guinea pig he was holding.

Ustinov suffered a devastating death, but the Soviets managed to profit from the mistake by harvesting Ustinov's organs for fresh samples of the virus. These proved to be even more powerful than the original strain. According to a former institute insider who wrote a book on his experience, Ken Alibek, the Soviets named it "Variant U" and sent it to be approved for use by the Soviet Defense Ministry in early 1990.

The Marburg virus is classed as a Category A bioterrorism agent by the Centers for Disease Control and Prevention, and **Kepler's** study was supported by the Defense Threat Reduction Agency, a Defense Department division established during the Manhattan Project era to combat weapons of mass destruction.

If the virus is ever deployed as biological warfare, the fruit bat's super-immunity may hold the answer to preventing its spread. But it may also go some way toward redeeming the bat in the eyes of the U.S. military — and could even make the animal an unlikely hero.

New compounds to treat RSV, Zika virus

New chemical compound shows promising antiviral activity

Original Article by Science Daily News, July 11, 2018

A new and promising class of chemical compounds has major potential for treating Zika virus and respiratory syncytial virus, or RSV, according to a new study by University of Alberta scientists. The next step is to develop a drug.

"This is both a remarkable scientific discovery and also something that has the potential to positively affect not only global health but also the economy of Canada," said Fred West, professor in the Department of Chemistry who led the new discovery along with David Marchant in the Department of Medical Microbiology and Immunology. The compound is similar to the naturally occurring isatisine A, an antiviral compound originally found in traditional Chinese herbal medicine.

Working in conjunction with Tom Hobman in the Faculty of Medicine & Dentistry, West and Marchant developed and then tested this chemical compound against powerful viruses, including RSV and Zika virus. The results were promising, showing that the chemical compound was active and effective against both viral infections.

Hobman is a professor of cell biology and an expert in the Zika virus, a pathogen that can cause serious prenatal defects in pregnant women that has been on the public radar since a major outbreak in May 2015.

Marchant is a professor of medical microbiology and an expert in RSV, which poses the biggest risk to infants, the elderly, and the immunocompromised. The virus can be responsible for more than 30 per cent of all hospitalized respiratory cases in any given year.

The next step of drug development is already underway. "What we aim to do is further refine this compound, to keep the elements that make it medically active and build in the structural components that make it possible for patients to consume in drug form," explained West. "We are approaching that point."

Journal Reference:

Bren Jordan P. Atienza, Lionel D. Jensen, Sarah L. Noton, Anil Kumar Victoria Ansalem, Tom Hobman, **Rachel Fearns**, David J. Marchant, F. G. West. *Dual Catalytic Synthesis of Antiviral Compounds Based on Metallocarbene–Azide Cascade Chemistry*. *The Journal of Organic Chemistry*, 2018; 83 (13): 6829 DOI: 10.1021/acs.joc.8b00222

Source: University of Alberta

NEIDL Researchers Create Tool to Study New Virus

Could help determine if Ebola-like LLOV can cause disease in humans

Original Article from The Brink, Pioneering Research from Boston University

By Sarah Reimer September 5, 2018

In recent years, traces of new zoonotic viruses—pathogens that live in animals and could potentially cause infectious diseases in humans—have been discovered in bats, fish, and other species around the world. But scientists have been stumped in their search for the complete genome for these viruses, the critical data that is needed to study their biology, and their potential dangers for humans.



Whitney Manhart (MED'20) (left) a PhD student in Elke Muhlberger's NEIDL lab, and lab manager Jennifer Pacheco are coauthors of a Cell Reports study about a tool that will help determine whether a new zoonotic virus, LLOV, can cause disease in humans. Photo by Jackie Ricciardi

But now, researchers at BU's National Emerging Infectious Diseases Laboratories (NEIDL) have created a tool that they say will unlock many of the mysteries of one of these new pathogens—a filovirus closely related to the Ebola and Marburg viruses—and help them determine whether it could cause disease in humans. Ebola and Marburg are among the most virulent and lethal viruses known to infect humans.

Called Lloviu virus (LLOV), the new filovirus was first discovered in 2002 in dead bats in a cave in Spain; it was found again in 2014, in dead bats in Hungary. It is not known whether LLOV sickened and killed the European bats (known as Schreiber's long-fingered bats, they are not found in North or South America) or if it causes disease in any animal. As with so many other new viruses, the complete genome has not been found.

The NEIDL team was led by **Elke Mühlberger**, a School of Medicine associate professor of microbiology, who is one of the world's leading filovirus researchers. Filoviruses are made up of single-stranded RNA instead of DNA.

Here is how **Mühlberger's** team created the new tool: They established a novel minigenome system for LLOV, which allows for the virus to be studied safely in a Biosafety Level-2 lab. Minigenomes are shortened versions of viral genomes, in which all the viral genes—those that cause infection—are removed and replaced by a

single nonviral reporter gene. Minigenomes contain all the necessary signals to replicate the virus in cells, but they lack the proteins necessary to produce infectious virus.

“However, in order to make a minigenome, you need the viral start and stop signals that allow for replication,” says Whitney **Manhart** (MED’20), a PhD student in **Mühlberger**’s lab, who coauthored with research study technician Jennifer **Pacheco** a September 4 *Cell Reports* [study](#) on the new tool. “These are exactly what we were missing from LLOV,” she says.

*“We currently have no therapeutics or vaccines which would target LLOV, and so answering basic questions about LLOV biology or the disease it might cause could help us be prepared for—or prevent—a major outbreak.” —Whitney **Manhart** (MED’20)*

To make up for the missing elements of the LLOV genome, the NEIDL researchers copied and pasted similar sequences from the related Ebola, Marburg, and Reston filoviruses (Reston causes disease in nonhuman primates, but is not known to cause disease in humans). This technique is called sequence complementation.

“While this work is most interesting to people who study filoviruses, the idea could be applied to any kind of virus,” Pacheco says, noting that researchers studying a bat-derived influenza with an incomplete genome used a similar method to create an infectious viral particle.

Pacheco, Manhart, and their colleagues found that LLOV replication and transcription mechanisms are more similar to Ebola viruses than Marburg viruses. “We found that when the start signal is the same as Ebola viruses, then LLOV can replicate well,” says **Pacheco**. “When the start signal is the same as Marburg viruses, LLOV cannot replicate.”

“The minigenome helps scientists answer some questions about LLOV,” **Manhart** says, “but we need the authentic virus to answer all questions.”

Using the LLOV minigenome system, **Manhart**, who has been trained to work in BSL-4 conditions, will produce the real virus in a BSL-4 facility. Then, she says, the virus can be used to study its potential to cause disease.

LLOV was found in bats that live in northern Africa, and across Europe, **Manhart** says. “So if a spillover did occur, it could infect a lot of people very quickly. We currently have no therapeutics or vaccines which would target LLOV, and so answering basic questions about LLOV biology or the disease it might cause could help us be prepared for—or prevent—a major outbreak. This minigenome system, and importantly, the infectious virus, will be critical in those studies.”

The other NEIDL researchers who helped develop the tool are PhD candidate Tessa Cressey (MED’19), research scientist Adam Hume, and former postdoctoral associate Laure Deflubé.

The work on the new tool was begun with support from the NEIDL director’s fund and is now funded by the NIH.

Old Drug, New Tricks

MED prof among researchers finding a modified malaria drug is effective at inhibiting Ebola

Original Article by The Brink, Pioneering Research from Boston University November 19, 2018

By Art Jahnke. Photos by Cydney Scott.

The inspiration stemmed from observations made during the 2014–2016 Ebola epidemic that swept through West Africa, infecting more than 28,000 people and killing more than 11,000 in Guinea, Liberia, and Sierra Leone alone. The outbreak attracted the attention of virologists from around the world, and several of them, including Robert Davey, noticed something intriguing: [patients with Ebola who had been treated with amodiaquine](#), an antiviral medication typically used to treat malaria, were 31 percent less likely to die.

“People were saying ‘It’s interesting’; I wondered if it was important,” says **Davey**, a School of Medicine professor of microbiology and a researcher at BU’s National Emerging Infectious Diseases Laboratories (NEIDL), who was working at the [Texas Biomedical Research Institute](#) at the time. “I thought we should test

some [chemical] derivatives and see if we could find some improvement over the amodiaquine performance,” he says.

Davey and collaborators set out to learn exactly which parts of the amodiaquine molecule were inhibiting Ebola virus infection. Their findings, published on November 3, 2018, in *Antiviral Research*, show that modified amodiaquine derivatives are significantly less toxic and nearly 10 times more effective at blocking Ebola virus than the original amodiaquine formula that greatly reduced mortality during the West Africa outbreak.

Blocking Ebola

To make the discovery, Davey teamed up with other virologists on the hunt for new therapeutics. Serendipitously, one of Davey’s colleagues from Japan—Yasuteru Sakurai, from the National Research Center for the Control and Prevention of Infectious Diseases in Nagasaki—knew another Japanese researcher, Masanori Baba of Kagoshima University, who had already made a series of amodiaquine derivatives in an effort to find new treatments for HIV and other viruses.

Davey says amodiaquine inhibits the two diseases, malaria and Ebola virus disease, in related ways. All cells need to get food from their surroundings. With malaria, amodiaquine prevents the parasite from digesting food from inside



NEIDL researcher Robert Davey has found that derivatives from a commonly used anti-malarial can prevent Ebola virus from entering cells.

red blood cells, so it basically starves to death. Ebola virus mimics food and tricks your cells into swallowing and trying to digest it. However, the virus senses this and uses it as a trigger to begin replication, avoiding digestion. So, by interfering with normal cell digestion, amodiaquine also blocks Ebola virus infection.

“With Ebola, we are affecting your own cell’s digestive system, but for a short time, which the cell can survive,” says Davey. “And the drugs that we developed likely improve targeting to places in the cell where Ebola virus likes to get to, whereas for malaria, the drugs are best at targeting the parasite’s feeding process, which it needs all the time. It’s a subtle difference in chemistry, but it’s important for making an effective drug treatment for patients.”

Davey used a high throughput screening plate with 384 wells to grow cells that were challenged with Ebola virus. A computer then analyzed the images to detect the most potent inhibitor of infection.

Working together at Davey's former lab in San Antonio, Tex., the team—which also included Masaaki Toyama of Kagoshima University and Norikazu Sakakibara of Tokushima Bunri University—tested nearly 70 amodiaquine derivatives, mixing each one with cells infected with Ebola virus and observing the effect that each derivative had on the live virus infection.

What they found, says Davey, was encouraging: 14 of the compounds tested did a better job inhibiting the Zaire strain of Ebola virus disease than straight amodiaquine. They also noticed that when two particular parts of the amodiaquine molecule were modified, the potency against the virus was further increased. Then, by combining the two features, they created further potent compounds, which appeared to completely prevent the virus from entering cells.

"If you combine those two things—less toxicity and better performance against the virus—you get something called a selective index," says Davey. "The selective index that we found easily met the criteria for clinical development."

Making moves

Since arriving at NEIDL, Davey and BU researchers Manu Anantpadma, a MED senior research scientist, and Patrick Keiser, a MED senior research technician, who joined Davey in the move from San Antonio to Boston, are taking the next steps on the long road of developing the discovery from "It's interesting" to an approved therapy. Next, Davey says, will come testing in animal models, as well as testing the potent compounds against other strains of Ebola virus.

Davey was drawn to BU, he says, by the opportunity to work at NEIDL, particularly in its BSL-4 lab, and because he has fond memories of Boston from years working as a postdoc on the Harvard Medical School campus.

"This is where I gained a passion for emerging infectious disease research and especially developing drug-based therapies," he says. "Boston is a hub for innovative scientific research and BU has great potential for new innovative opportunities through its excellent engineering, biomedical, chemistry, and traditional medicine programs. Also, my wife has always loved Boston and two of my three children were born here, so it is a type of homecoming for them. I am very happy to be here."

Davey also says he plans to continue his collaboration with Sakurai, Baba, Toyama, and Sakakibara, who are eager to work in the BSL-4 lab at NEIDL and who will be visiting the lab in the near future.

This work was supported by the [National Institutes of Health](#).

Researchers Develop Portable Diagnostic Test For Ebola And Malaria

Original from 90.9 WBUR Commonhealth, by Miriam Wasser, December 13, 2018

High fever, vomiting, diarrhea, abdominal pain: These are all early [symptoms of Ebola](#) hemorrhagic fever. They're also [symptoms of malaria](#), a mosquito-borne blood infection that's endemic in regions where Ebola tends to break out.

For public health officials working in West Africa during the [2014-2016 Ebola](#) outbreak, distinguishing between the two wasn't always easy, says Dr. John **Connor**, associate professor of microbiology and researcher at Boston University. Connor is part of an international team working on a portable, easy-to-use, battery-powered test that can identify Ebola, as well as malaria and other diseases, in less than 30 minutes.

"During the outbreak, one of the things that was, unfortunately, painfully obvious was that getting good diagnostics to the point that they were needed was difficult," he says. "[Our] goal was to make something really simple where you don't need a tremendous amount of training and people can pick it up very quickly. Current tests for Ebola are much more cumbersome, and for patients in rural areas, getting results can take days."



Prototype SERS reader and disposable tube containing reagents for differential diagnosis (Courtesy of Becton, Dickinson and Co.)

Connor's team, which includes the medical technology company Becton, Dickinson and Co., published a proof of concept research study in the journal *Science Translational Medicine* on Wednesday.

The test uses magnetic beads coated in antibodies that attract specific infectious agents in a blood sample and can be detected with a laser. When hit with the laser, each infectious agent creates what **Connor** calls “a unique scattering barcode” that is easily distinguishable.

By allowing health officials to diagnose a patient quickly and in a remote setting, this technology could have big public health implications in future out infectious disease outbreaks, he says.

Spotting Ebola in the Crowd

New field test can rapidly discern between the real thing and lookalike fevers

Original Article by The Brink, Pioneering Research from BU, January 28, 2019 By Kat J. McAlpine

At a clinic in Liberia, people trickle in from the surrounding neighborhoods, shivering despite the warm air, reporting varying degrees of headaches and nausea. Many of them are anxious—it's 2014 and an Ebola outbreak is underway and they fear the worst: that they, like some of their neighbors and loved ones, have contracted the highly fatal disease. One by one, they wait to be examined by a clinician, all the while mosquitoes float and buzz in the thick evening air.

During the early stages of Ebola, symptoms are often hard to distinguish from another disease endemic to the region, malaria, a mosquito-borne blood infection caused by a parasite. Without an instantaneous way of screening a patient's blood, people sick with malaria, instead of being treated with antimalarial medication, could be placed into quarantine and surrounded by other ill people who ultimately might, in fact, have Ebola and be highly contagious.

That danger of being unable to diagnose Ebola—or malaria—in seconds or minutes, rather than hours or days, is one of the major deficiencies that contributed to the 2014–2016 West Africa Ebola crisis, according to the Paul G. Allen Family Foundation.

“The standard diagnostic tests that exist are very good, but they're hard to do out in the field in the middle of an outbreak like we saw in West Africa,” says John **Connor**, a Boston University School of Medicine associate professor of microbiology. Instead, samples need to be sent to a facility capable of running the tests. “It could be several days between taking a sample and getting a diagnosis.”

When dealing with a fast-spreading, highly contagious, deadly disease like Ebola, those several days could mean the difference between containing an outbreak—or not.

Learning from the Past

Connor, in collaboration with researchers from Columbia University, the National Institutes of Health Integrated Research Facility, and clinical partners from Senegal and the Hemorrhagic Fever Lab at Université Gamal Abdel Nasser de Conakry, Guinea, as well as BD (Becton Dickinson), a global medical technology company, teamed up to do something about it. The international team, led by BD, proposed an idea for a new kind of diagnostic that would bridge critical gaps in the field. The Allen Foundation agreed to fund the idea.



“We set out to create a rapid, point-of-care diagnostic that could look for malaria, Ebola, and other pathogens that are often found in these regions,” says **Connor**, a virologist at the BU National Emerging Infectious Diseases Laboratories (NEIDL), which contains a Biosafety Level-4 laboratory that has been working with Ebola virus since August 2018.

As he reflects on the West Africa outbreak that prompted the last two years of his research efforts, **Connor** says better diagnostics are needed just as much now as ever. In the Democratic Republic of the Congo, **Connor** says, is “a smoldering outbreak...the largest outbreak that Congo has ever had and it’s looking like it’s not under control.”

John **Connor** says the SERS-based diagnostic system is reasonable to carry in a backpack. “I’ve put it in my backpack just to see,” he says. Photo by Mark Fleming

Ray of Light for Remote Clinics

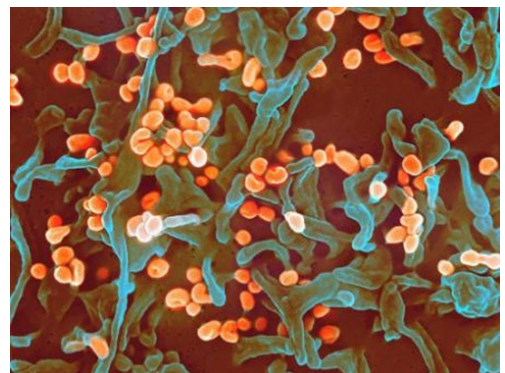
While there are myriad ways to design rapid, portable diagnostics, the solution pursued by the team was based on a test that could be stored without refrigeration, which is typically hard to maintain along supply routes to rural outbreak areas. That’s why a compact diagnostic system built on magnetic beads and glass-encased gold nanoparticles was so appealing for the job.

The system, surface-enhanced Raman scattering (SERS), is based upon the idea that light scatters off of different types of molecules in distinct ways. Specific molecules have distinct light-scattering signatures, or unique barcodes, that can be detected. Although the barcodes can be weak on their own, adding gold particles makes the barcode easier to detect by boosting the light signal.

“Gold amplifies the barcode by about a million times,” says Connor.

Partnering with BD, which had developed SERS for other global-health-related applications, **Connor** and his collaborators helped design a system that would be able to differentiate between various barcodes of the malarial parasite and Ebola virus, as well as Marburg and Lassa viruses, two other deadly hemorrhagic fevers found in the same regions of Africa where Ebola outbreaks occur.

At the start of the test, a small sample of blood is mixed with magnetic beads coated in antibodies that attract each of the four infectious agents. If the blood contains malaria-causing parasites or Ebola, Marburg, or Lassa viruses, the pathogens glom onto the magnetic beads. At the same time, similar antibodies on glass-encased gold nanoparticles also attach to the pathogens, creating a link between the magnetic and gold beads. Then, inside a small machine, the materials are concentrated into one spot by magnetic force and hit with a small laser beam.



Diagnosis in a Flash

Analyzing the barcode of light that flashes back from a sample, the machine provides a readout of the presence of malarial parasites or Ebola, Marburg, or Lassa viruses. If a sample contains more than one infectious agent, the test is able to identify them all.

Lassa virus is one of several hemorrhagic fevers endemic to parts of Africa, and like Ebola and Marburg, can sometimes be hard to distinguish from malaria infection. Image courtesy of NIAID

From sample-taking to final readout, the entire process can be completed in a half hour or less. The development of the system, and experimental data showing its efficacy in animal and human blood samples, was published December 12, 2018, in Science Translational Medicine.

According to one of the study’s coauthors, Yanis Ben Amor of Columbia University, who partnered with lab technicians in Africa to test the device in the actual field, a great benefit is that “once the sample is added to the tube, there is no need to reopen the tube since all the reagents are already inside.” For the technicians carrying out the testing, “this was seen as a tremendous advantage in the context of highly infectious samples.” Souleymane Mboup, an epidemiologist in Senegal and another co-author on the study, agrees. A key advantage of this platform, Mboup says, is its ability to detect multiple deadly infections all from a single patient sample contained within one test tube.

Designed to go anywhere, the system's components can be battery operated and can fit inside a backpack. How does **Connor** know that? He's stuffed them inside his own standard-sized backpack to test out its portability.

"The implications for getting good diagnostics to remote places are huge," says **Connor**, who is a corresponding author of the study.

Connor says that the value of the diagnostic goes beyond identifying who has a contagious illness and who does not. It's also about building stronger relations with the communities at risk of becoming infected.

During an outbreak, "there is a strain between clinicians who are trying to assist with limited resources and the local community that is losing trust in their healthcare workers because they don't have the appropriate tools and therefore can't help to their fullest capability," says Ben Amor.

If patients can rapidly be diagnosed and treated for illness, it can foster trust while immediately helping clinicians identify who should be quarantined and who should be sent home with antimalarial medicines.

The best scenario would be that clinicians are able to limit the time patients wait in crowded rooms, and therefore, decrease transmission opportunities, says Ben Amor.

Connor adds that the system could be custom-tailored to detect and differentiate virtually any combination of pathogens—bacterial, viral, fungal, or parasitic.

"The reason I find this system so promising is that it can diagnose more than one thing, which is important in the real-world context of infectious diseases," **Connor** says. "The disease landscape is complicated and pathogens aren't operating in isolation from one another."

Amid High-Profile Outbreaks, Benefit of Widespread Asymptomatic Screening Remains Low

Original Article by Contagion Live, FEB 14, 2019 | JARED KALTWASSER

When a West African Ebola outbreak overtook international headlines in 2014, the constant media attention was about more than the symptoms and consequences of the deadly virus. It was also about fear that the virus would spread far and wide.

Eleven people were treated for Ebola in the United States,¹ most of whom contracted the disease in West Africa, and all but 2 recovered. Although the outbreak's impact on Americans was infinitesimal compared with its impact in Sierra Leone and Liberia, the US cases caused outsized panic due to 1 factor: Ebola's famously long incubation period of up to 3 weeks. Americans knew the numbers were small, but what if those official numbers were hiding something much, much bigger?

CERTAINTY INSTEAD OF PANIC

On one hand, the 2014 Ebola episode is a cautionary tale about the dangers of public panics. On the other hand, it is an example of something epidemiologists cannot avoid: new emerging diseases are appearing—and evolving—in humans, and they are not all easy to detect or contain.

Recently, some researchers have begun asking the question of whether patients ought to be preemptively screened for diseases and other health problems after traveling overseas. John H. **Connor**, PhD, associate professor of microbiology at Boston University's School of Medicine and its National Emerging Infectious Disease Laboratories (NEIDL), said there are important reasons to get to the bottom of potential Ebola infections as soon as possible, particularly in the cases of health care workers who have traveled to Ebola outbreak zones and the family members or others with whom they have come into contact upon return.

"For both of these groups, having a test that can look for early signs of infection would be clinically useful because it would allow for more effective quarantine during the early stages of the disease and provide a level of fear reduction to those at risk," he said.

Dr. **Connor** is currently working on a test that can do just that. Last month, he and colleagues published findings in *Science Translational Medicine* showing that their rapid diagnostic test can detect antigens for Ebola, Lassa fever virus, and malaria in less than a half hour.²

“We undertook a study recently with colleagues at [the United States Army Medical Research Institute of Infectious Diseases] where we looked at the circulating immune response in nonhuman primates infected with Ebola virus,” he said.

The question was whether something could be identified in the primates’ immune responses that could positively identify a virus at work and differentiate it from other febrile diseases.

“Our work showed there are host responses, not viral RNA, that show up in the blood,” Dr. **Connor** said. “Importantly, these markers showed up prior to fever in many cases. We think that a test tracking these host responses would make early infection detection a possibility.”

WHOM TO TEST, AND WHEN?

Jesse Waggoner, MD, an assistant professor of medicine at the Emory University School of Medicine and Rollins School of Public Health, said a proactive approach (including pretravel health care) is the key to safe travel.

“Patients should have a low threshold to present to their medical practitioner or contact their travel medicine provider for any new illness that develops during travel or in the few months following their return,” said Dr. Waggoner, who also treats patients at Emory’s TravelWell clinic for pre- and postinternational travel health care. Patients who travel to countries with malaria, for instance, should seek medical attention even if fever is their only symptom and even if they took malaria prophylaxis prior to departure, he said.

Dr. Waggoner said gastrointestinal illnesses or respiratory infections are also common reasons for posttravel doctors’ visits. And while he said patients should tell their physician where they traveled, patients shouldn’t base their decision to see the doctor on where they traveled.

“The list of infections that we consider as providers will change based on where a patient has been, but individuals should not delay or forgo medical care because of travel to what is perceived to be a low-risk destination,” he said.

What about when there are no symptoms? Dr. Waggoner said that’s a question being studied, but at present, asymptomatic screening decisions need to be answered on a case-by-case basis.

“For common, short-term travel itineraries (days to a few weeks), screening is very low yield and is generally not recommended,” he said. “If individuals have prolonged exposure to freshwater or unsanitary conditions, screening for certain parasitic infections may be warranted.”

Waggoner added that patients who have sex with new partners while traveling might consider proactive testing for sexually transmitted infections. A number of studies have been performed in recent years looking into the efficacy of asymptomatic screening. They have shown little in the way of concrete benefit. For instance, a 2011 study that examined whether blood eosinophilia could indicate that a traveler had contracted schistosomiasis, strongyloidiasis, filariasis, and toxocariasis, showed the test, “appeared to be of no value in routine screening of asymptomatic travelers.”³

Another study, published in 2014, looked at the feasibility of using interferon gamma release assays (IGRAs) to screen patients for tuberculosis (TB) after long-term travel to countries where TB is endemic. They found that the screening could be used, but only 8 weeks after their return. And even then, widespread screening wasn’t necessarily worthwhile.⁴

“One might even argue that IGRA testing should be limited to only those travellers who are going to work in a medical setting,” wrote Floor Elfrink, MD, of the Dutch Public Health Service, and colleagues. In 2014, Dutch researchers also looked at whether routine screening of patients who undertook long-term travel (median time: 12 weeks) to the subtropics was a worthwhile way to detect parasitic infections. Although the study of 556 patients identified several infected patients, they found that routine screening for most of the parasitic illnesses was not warranted. When it came to schistosomiasis, detection rates were somewhat higher; they were also closely correlated with swimming in particular freshwater lakes in countries where the parasitic illness was endemic. Author

Darius Soonawalla, MD, PhD, concluded that such screening be limited to patients with a history of exposure to freshwater in highly endemic countries.⁵

The US Centers for Disease Control and Prevention (CDC) generally has no official position on whether to screen asymptomatic travelers for most diseases. Writing in the CDC’s most recent Yellow Book for international travel, Michael Libman, MD, of McGill University’s School of Medicine, Montréal, said there is little research on the cost-effectiveness of such screening, and he noted that it can be difficult to pin down risk

based on patient self-reports.⁶

“[E]xposure history is often unreliable and poorly predictive of infection, the value of a detailed itinerary is limited by incomplete information on where pathogens are endemic, and the type of travel often does not provide a practical assessment of risk,” he wrote.

Dr. Waggoner added that most general practitioners aren’t equipped with the tools or knowledge to screen for emerging diseases. Even though the workup for common symptoms can be done in a general outpatient setting, he said, “it is unrealistic and unfair to expect our general practitioners to remain current on outbreaks in foreign countries and know the appropriate testing for all potential travel-related infections.”

Waggoner said it’s better for patients to see a specialist, if possible, for posttravel illnesses.

PROGRESS FOR SPECIFIC, HIGH-PROFILE VIRUSES

Back at NEIDL, Dr. **Connor** said the technology he and his colleagues are developing could be used to effectively—and quickly—screen for a number of dangerous diseases, particularly those that initially “hide” in the liver and spleen, like Ebola, Lassa, and Marburg.

“These viruses often don’t enter the bloodstream in significant amounts until a lot of virus replication has gone on, so having earlier indicators of infection are important to find,” he said.

Still, Dr. **Connor** said these tests would be of primary benefit to people who had visited centers with outbreaks or to health care workers who had treated patients suffering from these infections.

“I think that administration to all returning travelers would likely be too complicated. It would most likely lead to large populations of travelers being tracked for a very low-probability event,” he said. “Focusing on travelers that are at high risk would likely be the best approach.”

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Education

In partnership with the Department of Microbiology and the GMS Immunology Training Program, the NEIDL co-sponsors the Microbial Pathogenesis and Immunology Seminar Series. Below is a list of virology guest speakers who presented at the NEIDL.

Date	Speaker	Title
26-Sep	Douglas Brackney, PhD Connecticut Agricultural Experimental Station	Navigating Anatomical Barriers to Transmission: An Arboviruses Tale
24-Oct	William Bishai, MD, PhD Johns Hopkins School of Medicine	M. tuberculosis host subversion: dampening a DAMP
7-Nov	Peter Daszak, PhD EcoHealth Alliance	Forecasting pandemics and the Global Virome Project
16-Nov	Wataru Kamitani, DVM, PhD Osaka University	Viral RNA recognition by Coronavirus nsp1
28-Nov	Samuel Behar, MD, PhD UMass Medical School	Tuberculosis: Recognizing the Problem
5-Dec	Mark Denison, MD Vanderbilt University	Inducing Infidelity as an Antiviral Strategy for MERS and Emerging Coronaviruses
23-Jan	Christopher Basler, Ph.D. Georgia State University	New Insights into Host Interactions with Ebola virus VP30 and VP35
30-Jan	Priti Kumar, Ph.D. Yale School of Medicine	Balancing Pathology and Protection in Flaviviral Infections of The CNS
20-Feb	Stephan Kissler, Ph.D. Joslin Diabetes Center	Type 1 Diabetes: Genes, Environment, and More Genes
27-Feb	Stefan Sarafianos, Ph.D. Emory School of Medicine	Targeting HIV and HBV with Novel Antivirals
6-Mar	Keith Jerome, M.D., Ph.D. Fred Hutchinson Cancer Research Center	Gene Therapy for Elimination of Persistent Viral Infections
13-Mar	Javier Irazoqui, Ph.D. UMASS Medical Center	The Novel Transcription Factor TFEB Integrates Metabolism, Innate Immunity, and Neural Signaling
20-Mar	Matthias Götte, Ph.D. University of Alberta	Active Site Inhibitors of Viral Polymerases: From HIV to Ebola
27-Mar	Paul Maglione, M.D., Ph.D. BU Pulmonary Center	Unraveling the Variable in Common Variable Immunodeficiency
10-Apr	Ya-Chi Ho, M.D., Ph.D. Yale School of Medicine	Single-cell Transcriptional Landscape Reveals Aberrant HIV-1 Host Interactions upon Latency Reversal
24-Apr	Donna Farber, Ph.D. Columbia University	Functional Regulation and Tissue Adaptation of Human T Cells
1-May	Danielle Clark, Ph.D. ACESO	The Host-Response to Severe Infection: Acute Disease and Long-Term Sequelae
1-Jun	Sangeeta Bhatia, M.D., Ph.D. MIT	Modeling hepatotoxic pathogens in engineered tissues
4-June	Dennis Carroll, Ph.D. US Agency for International Development	The Global Virome Project: the Transformative Power of Big Data

Partnership with BU EPIC Program

The EPIC student projects began with **John McCall's** October 2015 visit to the center to have some 3D printing done. John McCall, Director of IT, was introduced to David Campbell (the laboratory engineer) and William Hauser (Assoc. Prof. Mech. Eng.) and proposed a NEIDL student relationship and we began talks on developing a program.

The program was to have Dr. Hauser pick a team of Seniors to work with John to provide unique solutions to existing and emerging projects to enable better science. This group project would be done during their final semester and be presented to the Mechanical Engineer department annual project review.

We are now working with the fourth group of 5 students (Spring 2018), who continued the work began on the previous Capstone MRI Project. Their design altered the animal housing motor drive system from an electrically controlled system to a pneumatically controlled system using an available breathing air hose with regulated pressure in the MRI room in containment.

After this project, we are now into the 5th year of the program. Our experience has been that scope of the chosen projects and the time available for the students to complete them were not compatible. After a review of the student accomplishments, we both proposed and agreed that the students should be given the full year to work with the NEIDL projects, allowing for closer supervision on the development and implementation of the Senior Project solutions. This is scheduled to begin with the Fall 2019 class of Mechanical Engineering students.

NEIDL maximum biocontainment support at the NEIDL

It is not only essential to train research science staff to safely work in maximum biocontainment, it is also important to establish and maintain capability of operational support staff (non-research) to safely enter maximum biocontainment while active research is ongoing. Properly trained professional staff from Facilities, Information Technology and EHS groups is necessary in order to provide critical real-time support and repair functions for the research teams as necessary. Regulatory oversight personnel have also been trained for safe entry into maximum containment. The number of non-science research personnel with BSL-4 access has been intentionally developed for this specific purpose. As such, the NEIDL now has highly trained individuals who can uniquely support research efforts in BSL-4. These individuals are members of a very small club globally who are not researchers but are fully trained to safely enter and support needs of the science mission.

- The NEIDL Training Advisory Committee utilizes an in-house qualification assessment and reviews process and procedures related to steps and training criteria for all personnel to become authorized to work inside maximum containment
- We have a total of 44 NEIDL staff the BSL-4 access program:
 - 28 Science Staff
 - 6 EHS Staff
 - 2 Information Technology Staff
 - 6 Facilities/Maintenance Staff
 - 2 Boston Public Health Commission regulator training

During FY2019 alone, 16 new trainees entered the program, and 10 staff completed their individual mentored training plans.

Community Engagement

Engaging and sharing information with the community remains an important component of the NEIDL's mission. To succeed in this endeavor, the Community Relations Core ensures that the local community is informed in a timely, transparent and ongoing basis about the operations, safety, research and expertise of NEIDL personnel. We must continue and improve our efforts to inform and educate the community about WHAT we do and WHY, while at the same time building and sustaining community trust about the NEIDL and its mission. Below are the highlights from this past year's activities.

Community Liaison Committee (CLC)

The CLC continues to be an important group for promoting public participation and transparency at the NEIDL. Meetings are open to the public and provide an opportunity for key NEIDL personnel and researchers to provide regular updates on operational, regulatory, and scientific matters affecting the NEIDL. This year, Drs. Davey and Keusch spoke with the CLC about New Treatments for Ebola Virus and BU/ NEIDL collaborations locally, nationally and globally. BU held its first annual meeting to give a NEIDL update to the community. While this was not a regularly scheduled CLC meeting, a majority of the CLC members attended. In addition, we are thankful to CLC members as well as other stakeholders that supported our endeavors in person and by letter to amend the rDNA ban on BSL-4 research. These collaborative efforts resulted in the prohibition being lifted by the Boston Public Health Commission so that important research at BSL-4 could commence at the NEIDL. By taking advantage of the CLC's input, talents and expertise, we hope to ensure more effective communication and collaboration on engagement activities and programs involving the NEIDL and the community.

To ensure that community representatives continue to be involved in reviewing university wide research protocols submitted for approval; two members of the CLC sit on Boston University's [Institutional Biosafety Committee](#). Three members of the CLC volunteer their time and expertise to the Boston Biosafety Committee, the advisory group to the Boston Public Health Commission with respect to the BSL-4 permit and have agreed to continue to be resources as the need arises. As the CLC expands, other oversight groups will be interested in their knowledge and experience as additions to these committees.

Further, it should be noted that CLC members are invited, attend and participate in both tabletop and active simulated emergency response planning drills and exercises for the NEIDL with first responders (emergency, medical and other public safety personnel) to enable them to understand how emergency response procedures for incidents affecting the NEIDL are designed, implemented, evaluated, and improved. This year's exercises included a suspicious package, needle stick and work place violence.

Community Meetings

Representatives from the Community Relations Core are active in the community and serve as the face of Boston University in neighborhood and local business meetings as well as community events on a regular basis. We serve as members of various neighborhood business, safety and development committees. We sponsor and fund community activities either by the contribution of cash or through provision of University resources. This community presence allows us to identify and understand issues of neighboring residents, and answer questions in a timely manner.

Four of the events the NEIDL Community Relations Core sponsored this year are worth highlighting:

[Festival Betances Inquilinos Boricuas](#)

[South End Soccer](#)

[Orchard Gardens](#) Back to School Jamboree

[Innovation Night at Grove Hall](#), 5/9/2019, 575 Warren Street, Boston

Tours

The Community Relations team continues to plan, provide, and coordinate NEIDL tours. Tours regularly introduce community and other stakeholders to the NEIDL and reinforce the relevance of the facility, as well as the appropriateness of its location. During the summer months, requests to visit the NEIDL increase, providing greater opportunities to talk with high school and undergraduate students about career choices in a variety of different areas highlighting our NEIDL personnel. The addition of post docs as tour guides has proven informative and beneficial for both the guides and the attendees. Special thanks to Laura Avena and Sierra Downs from Dr. Griffiths lab for a wonderful NEIDL tour with the [BU STaRS](#) students. STaRS had an opportunity to talk with the researchers about education and career paths. The theme of the tour was one day in the life of a BSL-4 researcher. This tour generated a lot of dialogue between the students and NEIDL staff.

As part of a summer tour with a group of teenage girls interested in STEM participating in [GROW](#) – Greater Boston Research Opportunities for Young Women, we arranged for an all-female group of NEIDL researchers and staff to lead a panel discussion. This led to a very lively and frank exchange of advice and information. A special thank you to our volunteers this year: Laura Avena (Dr. Griffith's lab), Aditi Broos-Caldwell (Dr. Corley's lab), Shannon Benjamin (Environmental Health and Safety), and Fabiana Feitosa-Suntheimer (Dr. Colpitts lab).

Since 2012, we have led over 259 tours with approximately 3,600 local, national and international people visiting the NEIDL. From June 2018 through July 16, 2019, we conducted 17 tours with 376 attendees. From youth to retirees, all have been impressed with the facility and our willingness to answer questions and share information.

NBL-RBL Network Coordination

The NBL (National Biocontainment Laboratories) - RBL (Regional Biocontainment Laboratories) network is an organization of the NIAID funded centers from 13 academic research institutions, which promotes sharing of practices for improving the operations and safety of these biocontainment facilities. The NEIDL Community Relations staff collaborates regularly with other members of the NBL/RBL network via meetings, conferences and teleconferencing for sharing information on community activities of each member and adopting best practices learned during these interactions.

The annual meeting of the NIAID network of National and Regional Biocontainment Laboratories held their meeting this year in Galveston. Boston will be the host in 2020.

These meetings are always informative and a great way to meet and connect with colleagues from the regional and national laboratories. For Valeda Britton, Director of the Community Relations Core, and her National Galveston Lab counterpart, Connie Holubar, it was a good opportunity to sit with presenter, Mary Wooley who is the President and CEO of Research! America. We had an inspiring conversation about increasing public and elected officials' awareness of the benefits of research and building a solid citizen support base.

Educational Programs: Career Development

In connection with the NEIDL's mission to educate and train the next generation of scientists and in collaboration with BU's Medical Campus STEM efforts, the Community Relations Core put out a request for volunteers to participate in community engagement activities this Summer. The response has been amazing from all sectors of the NEIDL. From panelists, to tour guides to ID2 instructors and presenters, the NEIDL again demonstrated its commitment to exposing young community members to the excitement of science and research in this state-of-the-art building. Some of the highlights of community engagement activities are set forth below:

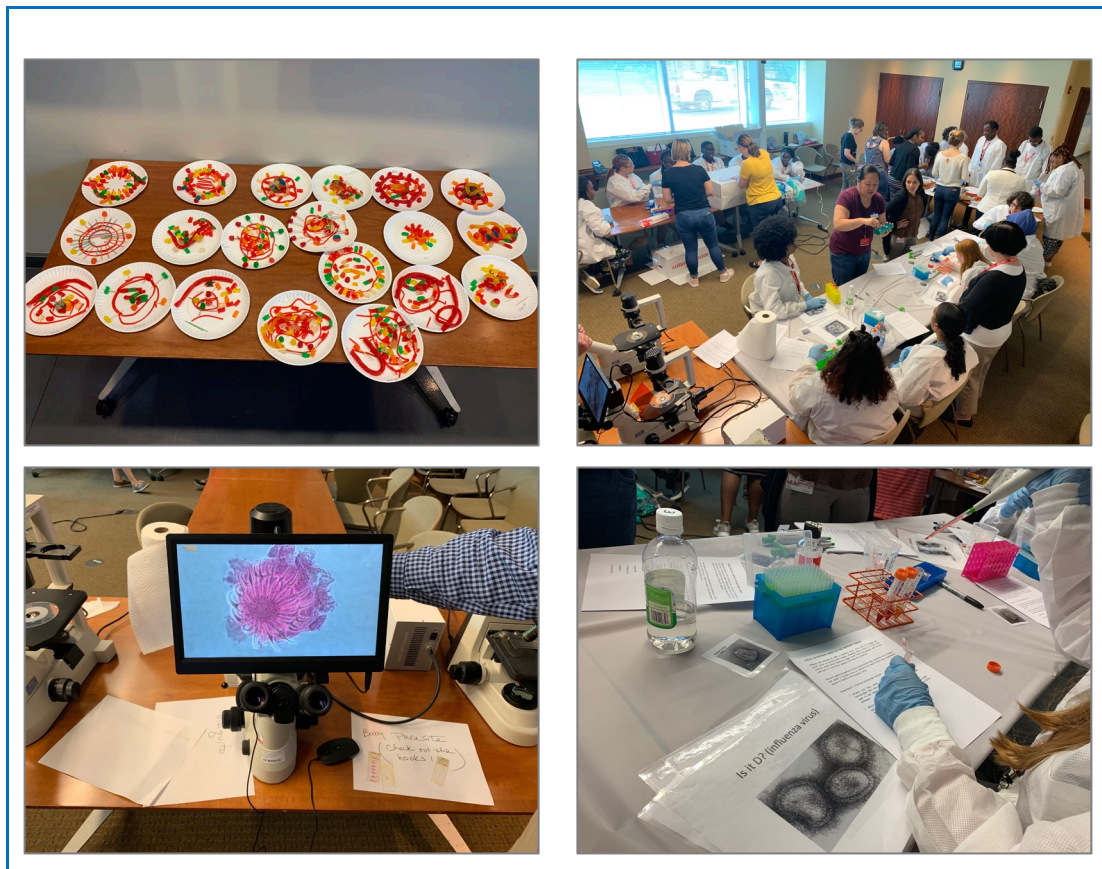
The NEIDL provided scholarships for three young women from local high schools near the BU Campus to attend a one-week BU sponsored program called Introduction to Careers in Medicine (ICM). Students attending ICM had presentations and hands on activities in the fields of Anatomy, Physiology, Microbiology, Surgery, and Emergency Medicine.

As part of the hands on/career exposure to Infectious Disease research, they participated in a revamped ID2 program. In the past, the ID2 audience and participants have been 7th graders. This year ID2 was in the NEIDL and the participants were high school students. Special thanks to EHS staff for their ideas, enthusiasm and support. Special, special thanks to Aditi, Judy, Callie, Victoria, Ellen, Whitney, Judith, and Jaime. Your commitment to ID2 and ICM was invaluable and much appreciated by the students.

As a result of this success, we decided to have the Boston Area Health Education Center (BAHEC) students try ID2 at the NEIDL. BAHEC is a program within the Boston Health Commission which is aimed at increasing diversity among Boston's healthcare workers. During last year's visit, the BAHEC students donned and doffed BSL-4 personal protective gear and engaged in manipulation exercises with marbles, pennies and macaroni. This year, they became virus detectives to solve a mystery virus affecting school children. This involved building a biosafety cabinet, identifying transmission paths, creating virus candy models, and doing DNA sequence analysis and Enzyme Linked Immunosorbent Assays (ELISA).

During the past year, students from Cumberland High School in Rhode Island visited the NEIDL as part of their introduction to the Medical Campus and its many educational/career opportunities. They spent time talking with staff in research, public safety and security, dental and saw the Blood Bank. This was their 4th tour of the NEIDL and we hope to see them again next year for their fifth trip to the campus.

Last, but not least, we gave seven scholarships to high students from public schools "in our backyard" to participate in a BU program called [SummerLab/CityLab](#). SummerLab allowed these students to have a hands-on week-long experience participating either in a class titled DNA, Genes and Drug Production or in a "mock" clinical trial of a new sickle cell drug.



"This has led me to expand my experiences in health care."



"Thank you for the opportunity to learn and broaden my career goals."

Facility Operations Activities

The Facilities Engineering Unit has had a busy year maintaining the critical infrastructure and updating systems that are approaching 10 years of operations. The combined efforts and management strategy of the Facilities Operations Group is to create and maintain unique and critical environments that will sustain the NEIDL science mission. Biocontainment function of the facility is critical. Strong links and collaborations with EHS, Public Safety and Research teams provides a practice of continuous monitoring and facility performance assurances that enables best practice and regulatory compliance. Major projects included:

- Building Automation System field panel upgrades were initiated as a multi-year project for migration to the latest technology and performance standards for continued vendor support.
- Effluent Decontamination System vent filter enhancements were installed to improve efficiency and safety of the effluent treatment process.
- Facilities along with the manufacturer, Progressive Recovery Incorporated, performed an Annual recertification on the EDS system and emergency vent filter skid.
- Facilities has implemented a BSL-4 lab space re-certification program to be performed on an annual basis. This will encompass a physical walk through of the lab space, whereby a detailed assessment is performed to evaluate the room from the standpoint of hvac, structural integrity, BAS alarming and overall general room condition. In addition an annual pressure decay of the space is performed.
- 3 Chillers were rebuilt as preventive maintenance due to age and manufactures recommendations to ensure operational capacity of the facility.



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